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(54) **Assay for aldehyde content**

(57) A composition, method, and device for quantitatively determining the concentration of an aldehyde in a sample are disclosed. The device includes a test pad having a suitable carrier matrix incorporating an indicator reagent composition capable of interacting with an aldehyde group in a compound to produce a detectable

and measurable response for aldehyde or dialdehyde compound. The indicator reagent composition can be incorporated into a carrier matrix, like filter paper, to provide a test pad useful in a dry phase aldehyde assay of a sample, especially for samples containing a high concentration of glutaraldehyde or formaldehyde.

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## Description

**FIELD OF THE INVENTION**

5 [0001] The present invention relates to a composition, method, and device for determining the concentration in a sample of a compound containing at least one aldehyde group. More particularly, the present invention relates to a method and device for assaying an aqueous sample for a compound containing at least one aldehyde group, having a concentration over the range of 0% to greater than 4%, by weight. In addition, the present invention also relates to a method and device for assaying an aqueous sample for a compound containing two or more aldehyde groups in a concentration of 0% to about 20%, by weight. The concentration of the aldehyde-type compound is determined by using an improved indicator reagent composition. Contrary to prior compositions, the present indicator reagent compositions have the advantage of quantitatively measuring a high range of aldehyde concentration in a sample without requiring multistep titration procedures. The present invention is particularly effective for determining the concentration of a monoaldehyde, such as formaldehyde, or a dialdehyde, such as glutaraldehyde.

**BACKGROUND OF THE INVENTION**

20 [0002] Compounds containing aldehyde groups have been used for many years in the medical sciences for various purposes. It is well known, for example, that formaldehyde, a monoaldehyde, and glutaraldehyde, a dialdehyde, are useful for fixing and preserving tissue specimens. In recent years, the role of compounds containing aldehydes in the medical community has expanded to that of a germicide useful for disinfecting or sterilizing medical instruments.

[0003] The use of formaldehyde and glutaraldehyde in disinfecting and sterilizing hemodialyzers is particularly common. Due to the proliferating reuse of hemodialyzers, the need for safe, accurate, and efficient methods of testing for disinfectant levels in the eluant of a hemodialyzer has increased dramatically.

25 [0004] Glutaraldehyde, in particular, also typically is used as a germicide for disinfection of other reusable medical devices, such as surgical instruments or endoscopes. The effective level of glutaraldehyde in commercial disinfection solutions generally ranges from about 1.5% to 3.5%, by weight of the solution. For example, CIDEX® 14 Day solution contains 2.4% glutaraldehyde as the active ingredient, and CIDEX® 28 Day solution contains 3.5% glutaraldehyde as the active ingredient.

30 [0005] The effectiveness of the germicidal solution depends on the concentration of the compound containing the aldehyde group. Currently, 2% glutaraldehyde and 4% formaldehyde, by weight, are used as germicidal solutions. These germicidal solutions are commercially available or can be manually prepared. The monitoring of the levels of compounds containing an aldehyde group in the solution is particularly important in assuring the effectiveness of the disinfectant. Unfortunately, the procedures presently available generally either require a multistep titration, lack accurate quantification, or involve complicated sample preparation, which hampers the convenience and efficiency of the assay.

35 [0006] For instance, several colorimetric procedures are available for the detection of trace amounts of formaldehyde. The detection ranges of currently available colorimetric procedures are extremely sensitive, i.e., detect formaldehyde concentrations in the range of parts per million (ppm), and are not suitable for the measurement of higher aldehyde concentrations in the weight percent (%) ranges. The test kits for these colorimetric assays, generally, are only available in an ampule format. The procedures commonly employ Schiff's reagent or Edgriwe's reagent as the indicator. Schiff's reagent, which is prepared from rosaniline and bisulfite in concentrated hydrochloric acid, and Edgriwe's reagent, which consists of chromotropic acid in strong sulfuric acid, both require strong acid. Typically, strong acids generally are avoided in a dry reagent strip test because the corrosive nature of the acids is not compatible with the carrier, typically cellulose, for the indicator reagent composition.

45 [0007] For the determination of percent levels of aldehyde compounds, particularly formaldehyde, the sodium sulfite and sodium bisulfite methods have been used. In these methods, the reaction of a sodium sulfite or sodium bisulfite reagent with formaldehyde generates an equal molar amount of sodium hydroxide. The amount of formaldehyde is estimated from the amount of acid required to titrate the generated sodium hydroxide. For a more thorough description of the sodium sulfite and sodium bisulfite methods, see J.F. Walker, "Quantitative Analysis of Formaldehyde," in *Formaldehyde*, 3rd ed., Reinhold Publishing Corporation, New York, NY, pp. 486-488 (1964). Though accurate, each method requires multiple steps leading up to the titration. In addition, the production of caustic sodium hydroxide makes it difficult to provide a quantitative dry reagent strip assay.

50 [0008] Organic nitrogen compounds, such as amines, amides, ureides, amino acids, and proteins having a hydrogen bonded to the nitrogen, also can react with formaldehyde to provide a useful assay for formaldehyde content. For example, formaldehyde reacts with lower amino acids, such as alanine, asparagine, and glycine in an aqueous solution. The aqueous solutions of these lower amino acids have a slightly acidic or neutral pH. In the presence of formaldehyde, however, the amino acids react as strong acids. The concentration of formaldehyde can be determined by end point

titration of the amino acid-formaldehyde solution with an alkaline solution. Further description of the reaction of formaldehyde with organic nitrogen containing compounds, and more particularly amino acids, can be found in J.F. Walker, "Reaction with Amines, Amides and Nitriles," in *Formaldehyde*, 3rd ed., Reinhold Publishing Corporation, New York, NY, pp. 359-414, in particular pp. 395-398 (1964).

5 [0009] Assays also are available for the determination of glutaraldehyde content. The reaction of glutaraldehyde with a mixture of sodium sulfite and an amine compound, for example glycine, is the subject of various U.S. patents. U.S. Patent Nos. 4, 521, 276 and 4,643,980 disclose a test system for glutaraldehyde consisting of a mixture having a defined ratio of sodium sulfite and an amine compound, in particular the amino acid glycine. The sodium sulfite and the amino acid react with glutaraldehyde to form a yellow-colored complex. In practice, the commercial product utilizing the principles described in U.S. Patent Nos. 4,521,376 and 4,643,980 involves a three-step reaction. First, glutaraldehyde is reacted with sodium sulfite to form a sulfite addition product and sodium hydroxide. Second, sodium hydroxide reacts with glycine to form sodium glycinate. Third, sodium glycinate reacts with another molecule of glutaraldehyde to form a yellow-colored addition product. The test strips based on this chemical sequence are "semi-quantitative" chemical indicators for use in determining whether the concentration of glutaraldehyde is above or below an established minimum concentration for a solution. The test strips are commercially available as the CIDEX® family of solutions test strips (Johnson & Johnson Medical, Inc., Arlington, Texas, U.S.A.).

15 [0010] The "semi-quantitative" test strip is a qualitative threshold test to determine whether the concentration of glutaraldehyde in a given sample meets a designated threshold. The test serves to indicate, either positively or negatively, whether the disinfectant solution contains a required minimum effective level of glutaraldehyde. A sample that contains the threshold level changes the color of the strip to yellow, indicating that the sample passes the assay. If the sample does not contain the threshold level of glutaraldehyde, the strip does not change to a yellow color, indicating that the sample fails the assay. The test does not provide a continuous quantitative assay of glutaraldehyde levels in the solution.

20 [0011] The reaction described in U.S. Patent Nos. 4,521,376 and 4,643,980 requires the use of both the sulfite and the amine compound to afford the desired color response. Neither patent discloses that an amino acid alone can form a chromophore, permitting quantification of an amount of aldehyde compound, particularly glutaraldehyde. In addition, neither patent discloses use of a diamino carboxylic acid in any assay, either quantitative or qualitative, for aldehydes, including dialdehydes.

25 [0012] Sodium sulfite and bisulfite methods as well as reactions with organic nitrogen containing compounds have been described for quantitative assay of aldehydes, but typically formaldehyde. These methods are tedious, and require a multistep titration to afford an accurate result. In addition, these reactions can generate strong base, such as sodium hydroxide, in sulfite/bisulfite methods, or, in the case of nitrogen containing compounds, the compounds, for example amino acids, can react as strong acids. The accurate quantitation of the strong acidic or basic component of the reaction is neither convenient nor feasible for a dry reagent test strip. A more thorough description of the sodium sulfite and sodium bisulfite methods can be found in J.F. Walker, "Quantitative Analysis of Formaldehyde," in *Formaldehyde*, 3rd ed., Reinhold Publishing Corporation, New York, NY, pp 486-488 (1964) Further description of the reaction of formaldehyde with organic nitrogen containing compounds, and more particularly amino acids, can be found in J.F. Walker, "Reaction with Amines, Amides and Nitriles," in *Formaldehyde*, 3rd ed., Reinhold Publishing Corporation, New York, NY, pp. 359-414, in particular pp. 395-398 (1964).

30 [0013] Other assays typically employed for detecting glutaraldehyde use chromogenic reactions to form a colored adduct, such as described in U.S. Patent No. 5,464,775. These reactions generally are used in a solution format assay for detecting glutaraldehyde in adult urine samples as evidence of urine adulteration. The assays require a chromogenic reaction of the aldehyde in a test sample with an aqueous carbonyl indicator, typically an aromatic azine or azide. These compounds are capable of forming a detectable chromogenic adduct. Examples of such indicator reagents named in U.S. Patent No. 5,464,775 include, for example, 2,4-dinitrophenyl hydrazine, 4-nitrophenyl hydrazine, hydrazine, phenylhydrazine, semicarbazide hydrochloride, and hydroxylamine. Generally, these compounds have conjugated or aromatic systems that allow for color formation.

35 [0014] Other commercially available test strips also are qualitative, rather than quantitative, indicators of whether the aldehyde concentration in the disinfecting solution is above a threshold level. For example, a commercially available test strip for formaldehyde allows for assay of formaldehyde levels between 2.5% and 4.0% in the disinfecting solution. The qualitative commercial test strips contain the hydrochloride salt of glycine, which releases hydrochloric acid as a product of the reaction with formaldehyde. The release of hydrochloric acid in solution causes a color change in a pH Indicator. These marketed strips are available under the trade name SERIM™ Formaldehyde Test Strips (Serim Research Corporation, Elkhart, Indiana, U.S.A.). In addition, the test strips do not provide a quantitative measurement of formaldehyde levels in the solution.

40 [0015] Reagent test strips also have been employed in testing steam sterilized products. The detection of formaldehyde vapor in dry or mixed steam is described in U.S. Patent No. 4,328,182. The strip disclosed in U.S. Patent No. 4,328,182 is a neutral, absorbent filter paper impregnated with an amino acid and a pH indicator. The strip is coated

with a hydrophobic coating to control uptake of formaldehyde vapor in order to detect high range formaldehyde concentration. The strip is not used for quantitative testing. There is no appreciation that a reagent test strip can be used for measuring the concentration of a gaseous aldehyde other than formaldehyde, for example glutaraldehyde. Moreover, there is no mention or recognition that an amino acid, or a mixture thereof, can be used in combination with a protein to prepare quantitative dry reagent test strips for assay of aldehydes in general, either in an aqueous solution or as a gaseous vapor.

[0016] To date, no known single assay is available to quantitatively assay aldehyde concentrations because the nonlinear relationship between the degree of pH change and aldehyde concentration is not yet sufficiently defined to provide a differentiable pH range relative to the aldehyde concentration in a sample. Moreover, no known single assay is available to quantitatively assay aldehyde concentrations based on the formation of a colored chromophore in an efficient, effective manner. Accordingly, it would be beneficial to provide an assay to analyze a test sample for aldehyde concentration in a simple, convenient dry test strip or solution format for detecting liquid or gaseous aldehyde concentration.

## SUMMARY OF THE INVENTION

[0017] The present invention is directed to a new and improved composition, device, and method of determining the aldehyde concentration in a test sample. A device includes a test pad comprising a suitable carrier matrix incorporating an indicator reagent composition capable of interacting with an aldehyde to produce a detectable response to aldehyde concentration. A carrier matrix of the test pad comprises a bibulous material, such as filter paper; a nonbibulous material, such as a strip, layer, or membrane of a polymerized material; or a mixture thereof. An indicator reagent composition is homogeneously incorporated into the carrier matrix, and the carrier matrix holds the indicator reagent composition homogeneously throughout the carrier matrix while maintaining the permeability of the carrier matrix to the sample.

[0018] In one embodiment, the present invention is directed to a method of assaying aldehyde content of an aqueous sample by utilizing a new indicator reagent composition. It has been demonstrated that a reagent composition including: (a) a protein, (b) an amine, (c) a color indicator, (d) an optional polymer, and (e) a carrier, for example water, affords excellent sensitivity to quantitatively assay a test sample for aldehyde content. The assay provides a method of determining the concentration of the aldehyde with sufficient color differentiation to quantitatively measure aldehyde concentration in the range of 0% to greater than 4% aldehyde, and particularly about 0.5% to greater than 4%, by weight, of the aldehyde, particularly aliphatic monoaldehyde and dialdehydes. The invention most preferably is used to detect levels of formaldehyde and glutaraldehyde concentrations in a dry test strip format.

[0019] In another embodiment, the present invention is directed to a method of assaying dialdehyde content of an aqueous sample by utilizing a new indicator reagent composition. It has been demonstrated that a reagent composition including: (a) a diamino carboxylic acid, (b) an optional polymer, and (c) a carrier, for example water, affords excellent sensitivity to quantitatively assay a test sample for dialdehyde content. The assay provides a method of determining the concentration of the dialdehyde with sufficient color differentiation to quantitatively measure a dialdehyde concentration of 0% to about 20%, and particularly about 0.5% to about 6%, by weight, of the dialdehyde, particularly an aliphatic dialdehyde. The present invention most preferably is used to detect levels of C<sub>2</sub>-C<sub>6</sub> aliphatic dialdehydes and, to achieve the full advantage of the present invention, to detect levels of glutaraldehyde.

[0020] An important feature of the present invention is to provide an accurate and reliable quantitative determination for the concentration of an aldehyde in a liquid, typically aqueous, or gaseous sample. The quantitative determination can be achieved in accordance with the invention by allowing a test sample containing a concentration of aldehyde to interact with the indicator reagent composition. The indicator reagent composition responds to the aldehyde content of the sample, even at a high concentration, to provide a differentiable color transition. Quantitative assay of the test samples is more sensitive and more accurate than achieved with previously disclosed compositions in that the indicator reagent composition is able to detect and differentiate between high levels of aldehyde present in the sample without titration or multistep sample handling.

[0021] Therefore, one aspect of the invention provides a method and composition for quantitatively determining the concentration of aqueous or gaseous aldehydes, including monoaldehydes and dialdehydes. A composition of the present invention interacts with the aldehyde group to produce a change in color of a device that is indicative of the concentration of the aldehyde in the sample.

[0022] Another aspect of the invention is to provide a method of assaying a test sample containing aldehyde group, said method having sufficient sensitivity and visual color resolution to allow differentiation between, and quantitative measurement of, samples having different concentrations of aldehydes, including monoaldehydes and dialdehydes, for example, glutaraldehyde and formaldehyde.

[0023] Yet another aspect of the invention is to provide a sensitive method of assaying samples for aldehyde concentration over the range of 0% to greater than about 4% by weight aldehyde, particularly in a dry test strip. The present method is especially useful in the detection of a high concentration of aldehyde, i.e., about 0.5% to greater than about

4% by weight aldehyde of the sample.

[0024] Another aspect of the present invention is to provide a sensitive method of assaying samples for dialdehyde concentration of 0% to about 20%, by weight, dialdehyde. The present method is especially useful in the detection of a high concentration of dialdehyde, e.g., about 0.5% to greater than about 6% by weight of the sample

5 [0025] Yet another aspect of the present invention is to provide an indicator reagent composition that interacts with an aldehyde group, and undergoes a visually or instrumentally differentiable color transition to allow determination of the aldehyde concentration in the sample.

[0026] In one embodiment, an aspect of the present invention is to provide a method of assaying the aldehyde content of a sample by incorporating an indicator reagent composition into a dry phase detection device, wherein the indicator reagent composition comprises: (a) a protein, (b) an amine, (c) a color indicator, (d) an optional polymer, preferably a cellulose-based polymer, and (e) a carrier, such as water.

10 [0027] In another embodiment, an aspect of the present invention is to provide a method of assaying the dialdehyde content of a sample by incorporating an indicator reagent composition into a dry phase detection device, wherein the indicator reagent composition comprises: (a) a diamino carboxylic acid; (b) an optional polymer, preferably a cellulose-based polymer; and (c) a carrier, such as water.

[0028] Still another aspect of the present invention is to provide a new and improved method of determining the aldehyde content of an aqueous sample by utilizing a test device, including a carrier matrix, said carrier matrix comprising a bibulous matrix, like filter paper, or a nonbibulous matrix, like a glass fiber or a layer of a permeable polymeric material, and said carrier matrix having incorporated therein an indicator reagent composition capable of interacting with an aldehyde present in the sample, to provide a color transition that can be correlated to the concentration of the aldehyde in the sample.

[0029] A further aspect of the present invention is to provide an improved dry phase test strip that incorporates an indicator reagent composition comprising (a) a protein, (b) an amine, (c) a color indicator, and (d) an optional polymer, and thereby provide a quantitative assay for the aldehyde content in a sample.

25 [0030] Yet another aspect of the present invention is to provide an improved dry phase test strip that incorporates an indicator reagent composition comprising (a) a diamino carboxylic acid, and (b) an optional polymer, and thereby provide a quantitative assay for the dialdehyde content in a sample.

[0031] Another aspect of the present invention provides a solution form of assay comprising (a) contacting a diamino carboxylic acid with a sample potentially containing a dialdehyde, (b) allowing the diamino carboxylic acid to react with any dialdehyde present in the sample, and (c) detecting a change in color or absorbance of the sample. In each aspect, the composition interacts with the aldehyde to produce a change in color of a device that is indicative of the concentration of the aldehyde content in the sample.

[0032] Yet another aspect of the invention provides a method and composition for quantitatively determining the concentration of aqueous or gaseous aldehyde, for example monoaldehydes and dialdehydes. An assay for determining dialdehyde content in a gaseous or vapor sample comprises the steps of (a) incorporating an indicator reagent composition comprising (i) a diamino carboxylic acid, and (ii) an optional polymer into a carrier matrix, and (b) exposing the indicator reagent composition to a gaseous sample potentially containing the dialdehyde.

[0033] The above and other aspects, advantages, and novel features of the present invention will become apparent from the following detailed description of the invention.

#### DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0034] In accordance with a method of the present invention, a quantitative assay of aqueous samples for aldehyde content, and especially high concentrations of an aldehyde, is accomplished, in one aspect, by utilizing an indicator reagent composition that includes (a) a protein, (b) an amine, (c) a color indicator, (d) an optional polymer, and (e) a carrier. By employing an indicator reagent composition of the present invention, sufficient sensitivity and sufficient visual color differentiation between samples of different aldehyde content is achieved. In accordance with the method of the present invention, in this embodiment, samples having an aldehyde content of 0% to greater than about 4%, and particularly about 0.5% to greater than about 4%, by weight of the sample, can be measured and differentiated.

50 [0035] To achieve the full advantage of the present invention, the method and composition are employed in dry phase, test pad assays to determine the concentration of an aldehyde in an aqueous solution or, alternatively, a gaseous vapor. The aldehyde commonly is a component of a germicide solution, for example glutaraldehyde or formaldehyde. A dry phase test strip, including a test pad comprising a carrier matrix incorporating an indicator reagent composition of the present invention, allows the rapid quantitative assay of samples by visual means.

55 [0036] In another aspect of the present invention, a quantitative assay of aqueous samples for dialdehyde content only, and especially high concentrations of a dialdehyde, in particular, is accomplished by utilizing an indicator reagent composition that includes (a) a diamino carboxylic acid, (b) an optional polymer, and (c) a carrier. By employing an indicator reagent composition of the present invention, sufficient sensitivity and sufficient visual color differentiation

between samples of different dialdehyde content is achieved. In accordance with the method of the present invention, samples having a dialdehyde content of 0% to about 20%, and particularly about 0.5% to about 6%, by weight of the sample, can be measured and differentiated.

[0037] In particular, the present invention allows determination of aldehyde concentration of the sample by the visual color change of a test pad on a test strip resulting from contact between the test strip and the sample. The aldehyde concentration of the sample is determined by correlating the detected color change to the aldehyde concentration of the sample. The test strip includes a test pad comprising an inert carrier matrix incorporating an indicator reagent composition. The present method allows rapid colorimetric determination of the aldehyde concentration of a sample, especially providing a suitable method for quantitatively measuring the concentration of the aldehyde, including monoaldehydes and dialdehydes, in aqueous solution.

[0038] Previous assay methods employed compositions that were unable to distinguish between aqueous solutions containing different concentrations of aldehyde above about 1.5%, by weight. The prior compositions utilized end point indicators without proteins, making discrimination between different pH levels induced by different concentrations of the aldehyde indistinguishable. In contrast, the present method can detect the content of aldehyde in the sample by utilizing an indicator reagent composition containing a protein that improves the overall quantifiable range of the aldehyde.

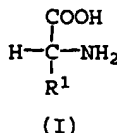
[0039] Previous assay methods also employed compositions that were unable to distinguish between aqueous solutions containing different concentrations of dialdehyde, particularly in the range of 1% to 2%, by weight. The prior compositions utilized end point indicators without varying color gradations, making discrimination between different concentrations of dialdehyde indistinguishable.

[0040] The method and composition of the present invention typically are employed in dry phase, test pad assays to determine the concentration of a dialdehyde in an aqueous solution or, alternatively, a gaseous vapor. The dialdehyde commonly is a component of a germicide solution, for example a glutaraldehyde solution. A dry phase test strip, including a test pad comprising a carrier matrix incorporating an indicator reagent composition of the present invention, allows the rapid quantitative assay of samples by visual means. In addition, the method of the present invention detects the content of dialdehyde in the sample by utilizing an indicator reagent composition that provides varying colors corresponding to different concentrations of the dialdehyde in solution, thereby improving the overall quantifiable range of the dialdehyde.

[0041] As described herein, one component of an indicator reagent composition of the present invention is a protein. Examples of suitable proteins are serum albumins, such as human serum albumin, bovine serum albumin, and ovalbumin; serum globulins, for example, gamma globulin; and the like. The proteins are protein fractions of blood serum which, when added to the indicator reagent composition, can improve the quantifiable range for detecting aldehyde concentration. Typically, the protein is present in the indicator reagent composition in an amount of about 1% to about 25%, and preferably about 3% to about 20%, by weight of the indicator reagent composition. To achieve the full advantage of the present invention, the indicator reagent composition contains about 3% to about 15% by weight of a protein.

[0042] The protein component is used in combination with an amine component of the indicator reagent composition to achieve a quantitative assay for the concentration of an aldehyde by correlating the change in pH with a color indicator. The amine component is present in the indicator reagent composition in an amount of about 5% to about 25%, by weight, and preferably about 10% to about 20%, by weight.

[0043] The amine compound typically is an amino acid, and more particularly a lower amino acid having a slightly acidic to neutral pH when dissociated in water. In preferred embodiments, the amine compound is an amino acid or peptide comprising at least two amino acids represented by the general formula:



wherein R<sup>1</sup> is hydrogen or alkyl optionally substituted with amino, guanidino, carboxy, hydroxy, ureido, or sulfhydryl. Preferably, the alkyl group is a straight chain alkyl group containing from about one to four carbon atoms.

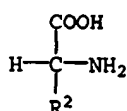
[0044] Nonlimiting examples of amino acids suitable for the invention are alanine, arginine, asparagine, aspartic acid, cysteine, glycine, glutamic acid, lysine, serine, threonine, ornithine, citrulline, and mixtures thereof. The preferred amino acids are lower amino acids, such as alanine, asparagine, and glycine. The amino acids commonly exist as a

weak acid and have a slightly acidic to a slightly basic when dissolved in water, about pH 5 to about pH 7.

[0045] As previously described; the amine group R<sup>1</sup> also can be a peptide. Peptides suitable for the invention comprise two to about 5 amino acids having a formula (I), as described above. A preferred peptide is glycylglycine.

[0046] The amount of amine compound for the invention preferably is from about 5% to about 25% amine compound, by weight of the composition. More preferably, the amount of amine compound comprises from about 10% to about 15%, by weight amine compound.

[0047] The diamino carboxylic acid utilized in an indicator reagent composition of the present invention typically comprise a lower (*i.e.*, C<sub>2</sub>-C<sub>6</sub>) carboxylic acid containing at least two amino groups and having a slightly acidic to neutral pH when dissociated in water. In preferred embodiments, the diamino carboxylic acid is represented by the general formula:



(II)

wherein R<sup>2</sup> is alkyl substituted with amino, amido, guanidino, ureido, and further optionally substituted with hydroxy. Preferably, the alkyl group is a straight chain alkyl group containing from one to about four carbon atoms.

[0048] Nonlimiting examples of diamino carboxylic acids suitable for the invention are lysine, ornithine, L-2,3-diaminopropionic acid, L-2,3-diaminobutyric acid, arginine, canavanine, hydroxylysine, asparagine, glutamine, and mixtures thereof. The preferred diamino carboxylic acids are lysine, ornithine, arginine, and mixtures thereof. The amount of a diamino carboxylic acid, either alone or in combination with the addition of other diamino carboxylic acids, in the present indicator reagent composition is about 1% to about 25%, by weight, and more preferably about 5% to about 15%, by weight of the composition.

[0049] As used herein, the term "alkyl" refers to a straight- or branched-chain hydrocarbon group, preferably containing about one to four carbon atoms, unless otherwise noted, which can be optionally substituted with one or more functional groups.

[0050] The term "amino" refers to a -NH<sub>2</sub> group.

[0051] The term "guanidino" refers to a -NH(C=NH)NH<sub>2</sub> group.

[0052] The term "carboxy" refers to a -COOH group.

[0053] The term "sulfhydryl" refers to a -SH group.

[0054] The term "hydroxy" refers to a -OH group.

[0055] The amino acids and peptides used in the invention can react with aldehydes, particularly aliphatic monoaldehyde and dialdehydes, to lower the pH of an aqueous solution. The term "aliphatic monoaldehyde or dialdehyde" refers to straight-chain hydrocarbon groups containing an aldehyde (-CHO) group, preferably containing from one to ten carbon atoms. More particularly, the term "monoaldehyde" refers to hydrocarbon groups containing one -CHO group. Likewise, the term "dialdehyde" refers to hydrocarbon groups containing two -CHO groups.

[0056] Diamino carboxylic acids used in the present invention can react with dialdehydes, particularly aliphatic dialdehydes. The term "aliphatic dialdehyde" refers to a straight-chain hydrocarbon group containing two aldehyde (-CHO) groups. The hydrocarbon group typically contains two to ten, and preferably two to six, carbon atoms. Examples of dialdehydes that can be assayed by the present method include, but are not limited to, oxalaldehyde, malonaldehyde, succinaldehyde, glutaraldehyde, and adipaldehyde. Commercially available products containing such dialdehydes include, but are not limited to, GLYOXAL® (oxaldehyde), CIDEX® (glutaraldehyde), CIDEXPLUS® (glutaraldehyde), OMNICIDE® 28 (glutaraldehyde), MAXICIDE® (glutaraldehyde), QUART® (glutaraldehyde), and WAVICIDE® -01 (glutaraldehyde).

[0057] To illustrate properties of the amino acids suitable for the present invention, aqueous solutions of amino acids, 10% by weight, were adjusted to a pH of 8.0 with sodium hydroxide. The change in pH of the solution was measured as formaldehyde and glutaraldehyde were added to the solution. The formaldehyde was added until about a 4%, by weight, solution was obtained. Glutaraldehyde was added until about a 2.5%, by weight, solution of glutaraldehyde was prepared. The pH shift of amino acid test solutions are summarized below in Table 1.

Table 1.

pH Shift of Amino Acids in the Presence of Aldehydes		
Amino Acid	Formaldehyde (4% by weight)	Glutaraldehyde (2.5% by weight)
Alanine	2.5	2.4
Glycine	3.8	3.8
Glycylglycine	3.8	1.2
Aspartic Acid	2.4	2.3
Glutamic Acid	1.9	2.1
Lysine	3.6	0.4
Arginine	2.4	0.5
Serine	2.5	2.1
Threonine	2.8	2.5
Cysteine	3.9	1.6

[0058] As demonstrated above, the pH of each solution drops in response to an increase in the aldehyde in the presence of an amino acid. However, in the absence of a protein, the change in pH in the presence of the amino acid varies sharply and is difficult to modulate. The addition of buffers, for example inorganic phosphate and borate buffers, can improve the quantifiable range of the aldehyde concentration. Organic buffers, such as tris(hydroxymethyl)aminomethane, also can be used to modulate the pH change. Both inorganic and organic buffers, however, have little effect on the overall spread of the quantifiable range.

[0059] The invention, therefore, in one aspect, comprises a combination of a protein and an amine in the indicator reagent composition. Without being limited to any theory, it is theorized that the amine group forms a neutral carbamino adduct with the aldehyde. The formation of the carbamino adduct releases a carboxylic acid from the amine as a free acid. The protein serves as a competitive substrate for the aldehyde or forms a gel-like barrier to prevent overreaction of the amine substrate with the aldehyde. Incorporating the protein into the indicator reagent composition allows for the quantification of the directly proportional relationship between the amount of aldehyde and the change in pH induced by the release of the carboxylic acid from the amino acid.

[0060] As such, it is possible to accurately quantify levels of aldehyde in the percent range using a dry reagent test strip instead of the parts per million range typically determined by titration. More particularly, glutaraldehyde concentrations of about 0.5, 1.0, 1.5, and 2.0% can be measured and differentiated. Formaldehyde concentrations of about 1, 2, 3 and 4% also can be measured and differentiated by the present invention.

[0061] Any protein that can function as a competitive substrate with the aldehyde or that can protect the reaction of the amine substrate from high levels of aldehyde content is suitable for the invention. By increasing or decreasing the concentration of the amino acid or peptide, the amine functionality of the amino acid or peptide can buffer the reagent system to achieve a desired gradient of pH changes. The use of the amino acid as the buffer has the added advantage in that, because the amino acid is both a substrate and a buffer, high amino acid concentrations will not diminish the sensitivity of the reagent system by reducing or narrowing the dynamic range of pH changes. Moreover, use of a single amino acid in the reagent composition eliminates unnecessary components and potential variables in manufacturing.

[0062] In addition to the protein component and the amine component, the indicator reagent composition contains a color indicator for distinguishing the change in pH. The pH of the solution decreases in a manner that can be quantitatively monitored by use of the color indicator. Preferably, the indicator is impregnated on a suitable carrier medium as part of the indicator reagent composition as described herein.

[0063] The color indicators suitable for the invention typically are pH indicators capable of undergoing a color change between about pH 3 and about pH 12, and more preferably between about pH 5 and about pH 11. Examples of pH indicators suitable for the invention include, but are not limited to, bromphenol blue, tetrabromophenol blue, Congo red, methyl orange, bromchlorophenol blue, p-ethoxychrysoidine, alpha-naphthyl red, sodium alizarinsulfonate, bromcresol green, 2,5-dinitrophenol, methyl red, lacmoid, litmus, chlorophenol red, benzoyl auramine G, azolitmin, bromcresol purple, bromphenol red, dibromophenol-tetrabromophenol-sulfonphthalein, p-nitrophenol, bromothymol blue, phenol red, neutral red, rosolic acid aurin, quinoline blue, cresol red, alphanaphtholphthalein, metacresol purple, ethyl bis[2,4-dinitrophenyl]acetate, tropaeolin, thymol blue, o-cresolphthalein, phenolphthalein, thymolphthalein, Nile blue A, alpha-naphtholbenzein, alizarin yellow GG, alizarin yellow R, and the like, or mixtures thereof. The preferred indi-



cators for the invention are methyl orange, bromocresol green, bromphenol red, methyl red, bromothymol blue, neutral red, cresol red, metacresol purple (alkaline range), thymol blue (alkaline range), thymolphthalein, and other indicators which typically undergo color change between from about pH 3 and about pH 10.5. More particularly the preferred indicator is methyl red, which indicates change in pH between from about pH 4.4 to about pH 6.2. Typically, the amount of color indicator for the composition is from about 0.005% to about 0.05%, by weight.

[0064] In accordance with the present invention, for example, the methyl red indicator is yellow at the high range of the pH concentration. A yellow color exhibited by the composition corresponds to the low range of the aldehyde concentration in the sample, about 0.5% and 1% of glutaraldehyde and formaldehyde, respectively. Conversely, at the low range of the pH concentration, the indicator is a pumpkin color or rose red color. Such colors correspond to the high range of the aldehyde concentration, about 2% and about 4% of glutaraldehyde and formaldehyde, respectively.

[0065] Diamino carboxylic acids also can be used in an indicator reagent composition of the present invention. To illustrate properties of the diamino carboxylic acids suitable for the invention, aqueous solutions of the diamino carboxylic acids (1% by weight) were prepared in a 2.5% glutaraldehyde solution containing 0.75 M sodium phosphate buffer. The pH of the solutions were adjusted to a pH of 8.0 with sodium hydroxide or hydrochloric acid. The absorbance of the solutions at 450 nm were taken after ten minutes with a spectrophotometer. For solutions having absorbance greater than 1.0, the solutions were diluted 10 or 20 times with water before the absorbance readings were taken. The absorbance of the test solutions are summarized below in Table 2.

Table 2.

Color formulation of Diamino Carboxylic Acids Reacting with Glutaraldehyde		
Diamino Carboxylic Acid	Absorbance (at 450 nm)	Solution Color
Lysine	12.80	Dark Brown
Ornithine	10.40	Dark Brown
L-2,3-Diamino-propionic acid	1.59	Yellow Brown
L-2,3-Diamino-butyric acid	0.06	Yellow
Arginine	1.49	Yellow Brown
Canavanine	0.48	Yellow
Hydroxylysine	5.85	Brown
Asparagine	1.45	Yellow Brown
Glutamine	4.60	Brown

[0066] The diamino carboxylic acids useful in the present invention can form color adducts, or complexes, having varying intensity. Some diamino carboxylic acids can provide a chromophore having a strong color intensity, as indicated by high absorbance value at 450 nm in Table 2, such as lysine, ornithine, and hydroxylysine. Other diamino carboxylic acids afford chromophores having weaker color intensity which is indicated by a low absorbance value at 450 nm in Table 2, for example, L-2,3-diaminobutyric acid, canavanine, asparagine, arginine, and L-2,3-diaminopropionic acid.

[0067] The present invention obviates the need to dilute a test sample prior to assay. For example, a test sample having a low dialdehyde content can be assayed using a diamino carboxylic acid having a low or high absorbance, but preferably a larger absorbance in order to achieve a sufficient color transition. A sample containing a higher dialdehyde content also can be assayed using a diamino carboxylic acid having a low or a higher absorbance, but a low absorbance diamino carboxylic acid may be preferred to eliminate the need to dilute the test sample in order to obtain differentiable color transitions.

[0068] The color differentiation also can be accomplished by increasing or decreasing the concentration of a diamino carboxylic acid. The amine functionality then can form a differentiable colored transition that is directly correlated to the amount of dialdehyde in the sample. In the case where the dialdehyde is glutaraldehyde, the preferred diamino carboxylic acids are lysine and ornithine, which have amino groups about the same distance apart as the aldehyde groups in glutaraldehyde.

[0069] One advantage of the present invention is that two or more diamino carboxylic acids can be combined to provide an indicator reagent composition that forms a colored chromophore of a desired intensity when reacted with the dialdehyde. The embodiment of the invention using diamino carboxylic acids need not be used in combination with a protein. A diamino carboxylic acid having a high absorbance value, for example, produces chromophores having intense color that can be combined with a diamino carboxylic acid having a weaker absorbance value to change the desired range for the intensity of the color response relative to the dialdehyde concentration. In this way, one skilled

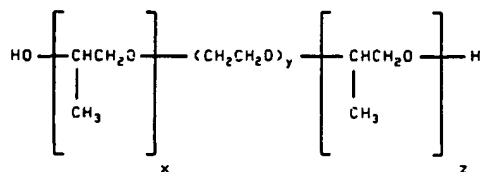
in the art can customize the indicator reagent composition to test a wide variety of dialdehyde concentrations. It is well within the skill of one in the art to vary the amount and identity the diamino carboxylic acids based on the properties, for example the absorbance, of the diamino carboxylic acids to provide a desired indicator reagent composition for the desired dialdehyde and range of dialdehyde concentrations.

**[0070]** An indicator reagent composition also can optionally contain a polymer. Preferably, the polymer is a neutral, nonionic polymer. The indicator reagent composition can contain a mixture of polymers to achieve a broad range quantitative assay, and particularly a high range quantitative assay, for aldehyde content. The preferred polymers are water-soluble, cellulose-based polymers. Other water-soluble polymers, such as polyvinylpyrrolidone, also can be used as the polymer in the present indicator reagent composition.

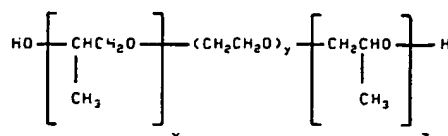
**[0071]** The water-soluble, cellulose-based polymers are derivatives of cellulose wherein hydroxy groups on the sugar moiety of cellulose are modified with a short chain alkyl (i.e., C<sub>1</sub>-C<sub>4</sub>), alkyl alcohol, or alkyl carboxylic acid. Examples of some common cellulose modifications are replacing a portion of the hydroxy groups with methyl, hydroxymethyl, hydroxyethyl, hydroxyethylmethyl, hydroxypropyl, hydroxypropylmethyl, or carboxymethyl groups, for example.

**[0072]** Examples of water-soluble cellulose-based polymers useful in the present invention include, but are not limited to, methylcellulose, hydroxymethylcellulose, hydroxyethylcellulose, hydroxyethylmethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose, carboxymethylcellulose and salts thereof, hydroxybutylcellulose, cellulose acetate, carboxymethylhydroxyethylcellulose, hydroxybutylmethylcellulose, and mixtures thereof.

**[0073]** In addition to cellulose-based polymers, other water-soluble polymers can be used in the method and composition of the present invention. Such water-soluble polymers are neutral, nonionic polymers, for example, polyvinylpyrrolidone, hydrolyzed polyvinylpyrrolidone, poly(vinyl alcohol), poly(vinyl acetate), vinyl acetate-vinyl alcohol copolymers, poly(methacrylamide), polyoxypropylene-polyoxyethylene block polymers having one of the following structures:



and



wherein x and z, independently, are an integer from about 4 to about 30, and y is an integer from about 4 to about 100, polyacrylamide, vinyl alcohol copolymers, and mixtures thereof.

**[0074]** The polymer is present in the indicator reagent composition in an amount of 0% to about 5%, and preferably about 0.1% to about 2%, by weight of the indicator reagent composition. To achieve the full advantage of the present invention, a water-soluble polymer is present in the indicator reagent composition in an amount of about 1% to about 2%, by weight of the composition.

**[0075]** The indicator reagent composition optionally can contain other chemically nonreactive ingredients. For example, one optional ingredient is a surfactant, in particular an anionic surfactant or a nonionic surfactant. The surfactant improves the ability of the sample to wet the carrier matrix, and the surfactant also improves the stability of the color transition of the indicator in response to the aldehyde.

**[0076]** The surfactant is present in the indicator reagent composition in an amount of 0% to about 1.5%, and preferably about 0% to about 1%, by weight of the composition. To achieve the full advantage of the present invention, the surfactant is present in an amount of about 0% to about 0.5% by weight of the composition.

**[0077]** Useful nonionic surfactants include, but are not limited to, an ethoxylated polysorbate, an ethoxylated alcohol, an ethoxylated phenol, i.e., an ethoxylated octylphenol, nonylphenol, or dodecylphenol with about 8 to about 30 moles

of ethylene oxide, a polyethylene glycol, e.g., PEG-8 through PEG-40, a polypropylene glycol, e.g., PPG-9 through PPG-34, an ethylene glycol-propylene glycol copolymer, e.g., a poloxamer, and similar nonionic surfactants, and mixtures thereof. In general, a useful nonionic surfactant has an HLB value of about 6 to about 25.

5 [0078] Anionic surfactants useful in the present invention are not particularly limited. Usually, the anionic surfactant includes a hydrophobic moiety, such as a carbon chain including about eight carbon atoms to about 30 carbon atoms, and particularly about twelve carbon atoms to about twenty carbon atoms; and further includes a hydrophilic moiety, such as sulfate, sulfonate, carbonate, phosphate, or carboxylate. Often, the hydrophobic carbon chain is etherified, such as with ethylene oxide or propylene oxide, to impart a particular physical property or reduced surface tension, to the anionic surfactant.

10 [0079] The anionic surfactants are well known, and can be a fatty acid, a salt of a fatty acid, an ethoxylated fatty acid, or a salt of an ethoxylated fatty acid, for example. Therefore, suitable anionic surfactants include, but are not limited to, compounds in the classes known as alkyl sulfates, alkyl ether sulfates, alkyl ether sulfonates, sulfate esters of an alkylphenoxy polyoxyethylene ethanol, alpha-olefin sulfonates, beta-alkyloxy alkane sulfonates, alkyl arylsulfonates, alkyl carbonates, alkyl ether carboxylates, fatty acids, sulfosuccinates, alkyl ether sulfosuccinates, sarcosinates, octoxynol phosphates, nonoxynol phosphates, taurates, fatty taurides, sulfated monoglycerides, fatty acid amido polyoxyethylene sulfates, and isothienates; or mixtures thereof. Many additional anionic surfactants are described in *McCutcheon's, Detergents and Emulsifiers, 1993 Annual*, published by McCutcheon Division, MC Publishing Co., and incorporated herein by reference.

20 [0080] The alkyl sulfates and alkyl ether sulfates are particularly effective classes of anionic surfactants. Examples of anionic surfactants useful in the composition and method of the present invention include, but are not limited to, the ammonium, monoethanolamine, diethanolamine, triethanolamine, isopropylamine, sodium, potassium, lithium, or magnesium salt of lauryl sulfate, dodecylbenzenesulfonate, lauryl sulfosuccinate, lauryl ether sulfate, lauryl ether carboxylate, lauryl sarcosinate, cocomethyl tauride, and sulfosuccinate half ester amide; or mixtures thereof. Examples of especially useful anionic surfactants are a lauryl sulfate salt, a lauryl ether sulfate salt, a lauryl phosphate salt, a sulfosuccinate salt, a dodecylsulfonate salt, a cholate salt, a C<sub>8</sub> to C<sub>18</sub> fatty acid, and mixtures thereof.

25 [0081] The carrier for the ingredients of an indicator reagent composition includes water. However, organic solvents, such as acetone, methanol, ethanol, isopropyl alcohol, ethylene glycol, propylene glycol, dimethylformamide, dimethylsulfoxide, acetonitrile, ethylacetate, and similar solvents, can be included in the carrier vehicle. The selection of a suitable organic solvent or solvents, in addition to water, to include in the carrier of the indicator reagent composition is within the capability of those skilled in the art of designing diagnostic assays.

30 [0082] The amount of organic solvent present in an indicator reagent composition generally is 0% to about 90%, and preferably about 10% to about 70%, by weight of the carrier. A carrier comprising water and an organic solvent, like methanol, ethanol, or acetone, is especially preferred because a carrier matrix impregnated with the indicator reagent composition can be dried within a few to several minutes.

35 [0083] The carrier matrix of the invention can be any substance capable of incorporating the chemical reagents required to perform the assay of interest, as long as the carrier matrix is substantially inert with respect to the chemical reagents. The carrier matrix also is porous or absorbent relative to the liquid sample.

40 [0084] The expression "carrier matrix" refers either to bibulous or nonbibulous matrices that are insoluble in the carrier of the indicator reagent composition and other physiological fluids and that maintain their structural integrity when exposed to the carrier and other physiological fluids. Suitable bibulous matrices include filter paper, sponge materials, cellulose, wood, woven and nonwoven fabrics, and the like. Nonbibulous matrices include glass fiber, polymeric films, and microporous membranes. Other suitable carrier matrices include hydrophilic inorganic powders, such as silica gel, alumina, diatomaceous earth and the like; argillaceous substances; cloth; hydrophilic natural polymeric materials, particularly cellulosic material, like cellulose beads, and especially fiber-containing papers such as filter paper or chromatographic paper; synthetic or modified naturally occurring polymers, such as cellulose acetate, polyvinyl chloride, polyacrylamide, polyacrylates, polyurethanes, crosslinked dextran, agarose, and other such crosslinked and noncrosslinked water-insoluble hydrophilic polymers. The carrier matrix can be of different chemical compositions or a mixture of chemical compositions. The matrix also can vary in regards to smoothness and roughness combined with hardness and softness. The handle usually is formed from hydrophobic materials such as cellulose acetate, polyethylene terephthalate, polycarbonate, or polystyrene. The carrier matrix is most advantageously constructed from filter paper or polymeric films.

45 [0085] The carrier matrix of the test strip can be any bibulous or nonbibulous material that allows permeation by the sample to saturate the test pad of the test strip that is impregnated with the indicator reagent composition. A preferred carrier matrix is a hydrophilic, bibulous matrix, including cellulosic materials, such as paper, and preferably filter paper. 50 The carrier matrix also can be a hydrophilic, nonbibulous matrix, including polymeric films, such as a polyurethane or a crosslinked gelatin. Such polymeric films possess all of the qualities required of a carrier matrix of the present invention, including suspending and positioning both the essential ingredients and any optional ingredients included in the indicator reagent composition, and permeability of the sample through the carrier matrix.

[0086] The present invention can be used to assay an undiluted sample for aldehyde concentration. As previously described, certain aldehydes, for example glutaraldehyde and formaldehyde, are commonly used to disinfect medical equipment, more particularly hemodialyzers, surgical instruments, and endoscopes. Most indicator reagent compositions cannot quantitatively assay undiluted samples for a high concentration of aldehyde because the pH spread cannot be differentiated and quantified. Most indicator reagent compositions can only qualitatively assay an aldehyde or dialdehyde. The qualitative assays detect only the presence of the disinfecting agent, i.e., either glutaraldehyde and formaldehyde, relative to an established threshold level.

[0087] Moreover, dry reagent test strips that are currently available on the commercial market detect only the presence of the disinfecting agent, i.e., either glutaraldehyde and formaldehyde, relative to an established threshold level. The commercially available dry reagent test strips cannot quantitatively determine the amount of aldehyde present in a sample.

[0088] In contrast, the present invention can be used to assay undiluted samples for aldehyde concentration over the range of 0% to greater than about 4%, and especially about 0.5% to greater than about 4%, by weight, of the composition. This capability greatly increases versatility of the invention because medical workers often use aldehyde-containing germicide solutions to sanitize hemodialyzer units. The effectiveness of the germicide solutions is directly dependent on the concentration of aldehyde in the sample. The composition of the invention, therefore, can be used by medical personnel as a test for quantitatively identifying the amount of a compound containing an aldehyde group in a sample either as an aqueous solution or as a gaseous vapor. In particular, the change in pH of an aqueous solution can be measured by incorporating the composition into a dry reagent test strip or by using the composition as an indicator solution.

[0089] The indicator reagent composition undergoes a color transition upon contact with the sample to provide an assay for aldehyde concentration from the intensity and degree of the color transition. The indicator reagent composition of the present invention provides a sufficiently resolved and differentiated color transition such that the aldehyde content in the sample can be measured and accurately determined without the use of color-measuring instruments, such as spectrophotometers or colorimeters, over a concentration range of 0% to greater than about 4%, by weight, of the composition for aldehydes, and about 0% to about 20%, by weight, of the composition for dialdehydes. If desired, such color-measuring instruments can be used to measure the difference in color degree and intensity between the sample and a solution having a known concentration of aldehyde.

[0090] The intensity and degree of the color transition are used to determine the aldehyde content of the sample by comparing or correlating the color produced by the sample to colors produced by solutions having a known aldehyde concentration. In accordance with an important feature of the present invention, the indicator reagent composition provides a sufficiently resolved and differentiated color transition such that the aldehyde content of an undiluted sample can be measured for an aldehyde content of 0% to greater than about 4% by weight without the use of color-measuring instruments.

[0091] For dialdehydes in particular, differentiation of color can assay a dialdehyde content of about 0% to about 20%, by weight, in an undiluted sample. An indicator reagent composition of the present invention, as described above, can be used in dry phase, test pad assays for aldehyde. The dry phase, test pad assay for aldehyde utilizing a present indicator reagent composition is performed in accordance with methods well known in the art. In general, the assay for aldehyde is performed by contacting the sample with an indicator reagent composition, which typically is incorporated into an analyte detection device. In one method, the analyte detection device is contacted with an aqueous sample by dipping the analyte detection device into the aqueous sample. Alternatively, the aqueous sample can be applied to the analyte detection device dropwise. The resulting change in color of the analyte detection device reveals the aldehyde concentration of the sample; and, if so designed, the resulting color transition can be compared to a standardized color chart to provide a measurement of the aldehyde concentration of the sample.

[0092] Typically, the analyte detection device is a test strip impregnated with an indicator reagent composition, designed either as a single pad test strip (to assay only for a single analyte) or as a multiple pad test strip (to assay for several analytes simultaneously). For either type of test strip, the test strip includes a support strip, or handle, normally constructed from a hydrophobic plastic, and a reagent-test pad, comprising a bibulous or nonbibulous carrier matrix. In general, the carrier matrix is an absorbent material that allows the liquid sample to move in response to capillary forces through the matrix to contact the indicator reagent composition and produce a detectable and measurable color transition.

[0093] In accordance with one method of the present invention, to perform a dry phase test strip assay for aldehyde, an aqueous solution, including: (a) about 3% to about 25%, by weight, of a protein; (b) about 5% to about 25% by weight of an amine; (c) about 0.005% to about 0.05% by weight of a color indicator; (d) about 0.2% to about 5% by weight of a polymer, like a cellulose-based polymer; and (e) any other desired optional ingredients, or solvents, first is prepared. A nonbibulous matrix, such as a polyurethane film, or a bibulous matrix, such as filter paper, then is saturated or impregnated with the aqueous solution by immersing or by spraying the aqueous solution onto sheets or precut strips or pads of the polyurethane film or filter paper.

- [0094] After removing the aqueous solvent by drying in a forced air oven at a temperature of about 40°C to about 100°C for about 2 to about 15 minutes, the impregnated polyurethane film or filter paper, if necessary, is cut to an appropriate size, such as a pad having dimensions from about 0.2 in. (inch) (0.5 cm) by about 0.5 in. (1.3 cm) to about 0.5 in. (1.3 cm) by about 1 in. (2.5 cm).
- 5 [0095] In another example, such as to perform a dry phase test strip assay for dialdehyde, an aqueous solution, including: (a) about 1% to about 25% by weight of a diamino carboxylic acid; (b) about 0% to about 5% by weight of a polymer, like a cellulose-based polymer; and (c) any other desired optional ingredients, or solvents, first is prepared. A nonbibulous matrix, such as a polyurethane film, or a bibulous matrix, such as filter paper, then is saturated or impregnated with the aqueous solution by immersing or by spraying the aqueous solution onto sheets or precut strips
- 10 or pads of the polyurethane film or filter paper.
- [0096] Then, after removing the aqueous solvent by drying in a forced air oven at a temperature of about 40°C to about 100°C for about 2 to about 15 minutes, the impregnated polyurethane film or filter paper, if necessary, is cut to an appropriate size, such as a pad having dimensions from about 0.2 in. (inch) (0.5 cm) by about 0.2 in. (0.5 cm) to about 0.2 in. (0.5 cm) by about 1 in. (2.5 cm).
- 15 [0097] An impregnated reagent paper can be used as an indicator strip in a steam sterilization process. When a medical device is sterilized with aldehyde vapor, such as formaldehyde or glutaraldehyde, exposure to the vapor causes the reagent paper to change color. The color gradations can be compared to predetermined colors correlating to known quantities of aldehyde in order to determine whether the aldehyde content in the solution is sufficient for effective sterilization.
- 20 [0098] The intensity and degree of the color transition are used to determine the aldehyde content of the sample by comparing or correlating the color produced by the sample to colors produced by solutions having a known aldehyde concentration. In accordance with an important feature of the present invention, the indicator reagent composition provides a sufficiently resolved and differentiated color transition such that the aldehyde content of an undiluted sample can be measured for an aldehyde content of 0% to about 4%, by weight, aldehyde, or for dialdehydes in particular, for
- 25 a dialdehyde content of 0% to about 20%, by weight, dialdehyde, without requiring the use of color-measuring instruments.
- [0099] It should be understood that it is well within the experimental techniques of those skilled in the art of preparing test devices to determine the proper balance between size of the test pad, the strength of indicator reagent composition solutions, the amount of sample, and the method of introducing the sample to the test strip, such as by pipetting rather
- 30 than dipping, in order to design a quantitative assay for aldehyde content utilizing the method and composition of the present invention.
- [0100] Dried, impregnated polyurethane film or filter paper then is secured to an opaque or transparent hydrophobic plastic handle with double-sided adhesive tape. The resulting test strip then is contacted with a sample for a sufficient time to saturate the test pad with the sample. After waiting a predetermined time, such as from about 1 to about 120
- 35 seconds, the test strip is examined, either visually or by instrument, for a response. The color transition, if any, of the test pad reveals the concentration of aldehyde in the sample.
- [0101] In many cases, simple visual observation of the test strip provides the desired information. If more accurate information is required, a color chart bearing color spots corresponding to various known concentrations of aldehyde can be prepared for the particular indicator reagent composition used in the test strip. The resulting color of the test
- 40 strip after contact with the sample then can be compared with the color spots on the chart to determine the concentration of aldehyde in the sample. If a more accurate determination is required, a spectrophotometer or colorimeter can be used to more precisely determine the degree of the color transition. In addition, the dry phase test strip assay can be made quantitative by employing spectrophotometric or colorimetric techniques, as opposed to visual techniques, in order to more reliably and more accurately measure the degree of color transition, and, therefore, more accurately
- 45 measure the concentration of aldehyde in the sample.
- [0102] The amount of aldehyde can be detected in a gaseous vapor, for example as a component of sterilizing steam treatment or as a vapor mix, such as a formaldehyde vapor mix. To measure the aldehyde content of the gaseous sample, the analyte detection device is directly exposed to the gaseous medium containing the aldehyde by, for example, suspending the device in the medium.
- 50 [0103] In one example, the indicator reagent composition can be impregnated on reagent paper, i.e. filter paper, and used for the detection of formaldehyde or glutaraldehyde in the air. The aldehyde reacts with the indicator reagent composition causing a color change in the paper. The change in color can be compared with predetermined color gradations that correlate to known quantities of aldehyde.
- 55 [0104] The use of spectrophotometers and colorimeters is particularly useful, however, in a solution format of the test, preferably for determining dialdehyde content. In a solution-based assay, a liquid sample can be treated with the indicator reagent composition, typically in a carrier. The sample and indicator reagent composition are allowed to interact, forming a colored chromophore, which can be detected or analyzed with a calibrated colorimeter. Also, a spectrophotometer can be used to measure the absorbance of the treated sample. In the case of a solution containing

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glutaraldehyde, the reaction of glutaraldehyde with lysine or ornithine yield a color solution having a strong absorbance in the range of from about 300 nm to about 500 nm. Colorimetric or spectrophotometric data obtained from the treated sample can be compared with a standard curve constructed using solutions having known quantities of dialdehyde, for example glutaraldehyde.

[0105] In accordance with various embodiments of the present invention, the following dry phase test strips were prepared for a two-fold purpose: (1) to illustrate a test strip of the invention and (2) to demonstrate the effectiveness of the indicator reagent composition. All amino acids, diamino carboxylic acids, buffers, proteins, pH indicators and other reagents were purchased from Sigma-Aldrich (St. Louis, Missouri, U.S.A.), where possible. Cellulose-based polymers were purchased from Aqualon Company (Wilmington, Delaware, U.S.A.).

## **Example I**

[0106] Solutions having the following components listed in Table 3, below, were prepared in water and adjusted to pH 7.9 with sodium hydroxide. Filter paper, such as Schleicher & Schull #903 absorption paper, was immersed in a solution to impregnate solution components onto the paper. Excess solution was removed from the surface of the filter paper with a scraper bar.

Table 3

Indicator Reagent Composition Amount of Ingredient (Weight % of solution)		
Ingredient	Strip A (comparative)	Strip B
Bovine Serum Albumin	--	5%
Glycine	20%	20%
Methyl Red	0.01%	0.01%
Hydroxyethylcellulose	0.2%	0.2%

[0107] The filter paper was dried at 65°C for 10 to 20 minutes in a forced-air oven. The dried impregnated filter paper was backed with double-sided adhesive, and slit into 0.2 inch (0.5 cm) wide ribbons. A ribbon of filter paper incorporating the indicator reagent composition of the present invention then was attached to a polystyrene plastic support (10 mil) by means of the double-sided adhesive. The plastic support, including the saturated or impregnated filter paper, was slit into 0.2 inch (0.5 cm) wide strips. Accordingly, the plastic support included a pad having dimensions of saturated or impregnated filter paper to provide a test pad comprising a filter paper carrier matrix incorporating an indicator reagent composition of the present invention.

[0108] A stock solution of 37% formaldehyde was diluted with deionized water to concentrations of 1, 2, 3 and 4% to obtain a series of test solutions. The prepared strips were dipped into the series of test solutions. The excess was removed by touching the side of the strip with a paper absorbent, for example a paper towel. The color of the treated portion of the test strip was recorded after 60 seconds. The color response of each impregnated strip is shown below in Table 4.

Table 4

Color response of dry reagent strips containing Indicator reagent composition without protein versus with protein to increasing formaldehyde concentration		
Formaldehyde Concentration	Color Response of Dry Reagent Strip	
	Strip A (comparative)	Strip B
1%	Yellow	Yellow
2%	Rose Red	Orange
3%	Rose Red	Pumpkin
4%	Rose Red	Rose Red

[0109] Using similar procedures as the steps required to prepared the test formaldehyde procedures, a stock solution of 25% glutaraldehyde was diluted with deionized water to concentrations of 0.5, 1.0, 1.5 and 2.0% to give a series of test solutions. The test solutions were tested with the prepared strips and the results are reported below in Table 5.

Table 5

Color response of dry reagent strips containing indicator reagent composition without protein versus with protein to increasing glutaraldehyde concentration		
Glutaraldehyde Concentration	Color Response of Dry Reagent Strip	
	Strip A (comparative)	Strip B
0.5%	Orange	Yellow
1.0%	Rose Red	Lemon
1.5%	Rose Red	Orange
2.0%	Rose Red	Pumpkin

[0110] In particular, the data in Tables 4 and 5 demonstrate that the presence of the protein, bovine serum albumin, in the indicator reagent composition greatly improves the overall quantitation range of the aldehyde. This principle is evidenced by the comparison between comparative dry reagent Strip A, containing no protein, and the dry reagent Strip B, containing 5% protein in the reagent indicator composition. The strip containing the protein exhibits a unique color at each quantitation level, whereas the strip without protein detected only a differentiation at the 0.5% and 1.0% levels of glutaraldehyde concentration, and the 1% and 2% levels of formaldehyde concentration. The increased ability to differentiate a particular pH over the pH range is an important advantage for identifying and quantifying aldehyde content in a sample, and is quite unexpected in light of the present state of the art.

#### Example II

[0111] The procedure for preparing the solution of Strip B above, as described in Example I, was repeated except substituting 5% by weight protein, bovine serum albumin, for the following concentrations of the desired proteins. For the preparation of Strip C, 3.8% by weight human serum albumin was substituted for the 5% by weight bovine serum albumin. For the preparation of Strip D, 20% by weight ovalbumin was substituted for the 5% by weight bovine serum albumin. For the preparation of Strip E, 20% by weight gamma globulin was substituted for the 5% by weight bovine serum albumin. Each solution was used to prepare impregnated strips in a manner in accordance with Example I, except substituting the solutions for Strip C, Strip D and Strip E for the solution used to prepare Strip B. The concentrations of protein in the solutions for the preparation of each strip are summarized below in Table 6.

Table 6

	Strip C	Strip D	Strip E
Protein Concentration	3.8% Human Serum Albumin	20% Ovalbumin	20% Gamma Globulin

The color response of the impregnated strips was tested according to the procedures described above in Example I for the assay of the formaldehyde test solutions. The results are reported below in Table 7.

Table 7

Color response of indicator reagent composition to increasing formaldehyde concentration			
Formaldehyde Concentration	Color Response of Dry Reagent Strip		
	Strip C	Strip D	Strip E
1%	Orange	Orange	Tangerine
2%	Tangerine	Tangerine	Pumpkin
3%	Pumpkin	Pumpkin	Rose Red
4%	Rose Red	Rose Red	Rose Red

[0112] The impregnated strips were additionally tested according to the procedures described above in Example I for the assay of the glutaraldehyde test solutions. The results are reported below in Table 8.

Table 8

Color response of Indicator reagent composition to increasing glutaraldehyde concentration			
Glutaraldehyde Concentration	Color Response of Dry Reagent Strip		
	Strip C	Strip D	Strip E
0.5%	Yellow	Yellow	Lemon
1.0%	Lemon	Lemon	Orange
1.5%	Orange	Orange	Pumpkin
2.0%	Pumpkin	Pumpkin	Pumpkin

[0113] The results summarized in Tables 7 and 8 show the effectiveness of proteins in addition to bovine serum albumin when incorporated in a composition of the invention. As shown above in Tables 7 and 8, human serum albumin, ovalbumin, and gamma globulin demonstrate a unique color response at all or nearly all levels of the quantitation ranges for glutaraldehyde and formaldehyde, respectively.

[0114] The results set forth in Tables 4, 5, 7 and 8 show that a test strip of the present invention is capable of assaying for aldehyde content over an entire range of 0% to greater than 4% by weight. More specifically, the data show that the invention can provide a quantitative determination for a formaldehyde concentration range of from about 1% to about 4% by weight of the total weight of the sample and for a glutaraldehyde concentration range from about 0.5% to about 2.0% by weight of the total weight of the sample.

[0115] From the visual assays and the data presented in Tables 4, 5, 7 and 8, it has been demonstrated that an indicator reagent composition of the present invention accurately assays for high levels of aldehyde, directly and quantitatively. In preferred embodiments, the composition contains a mixture of lower amino acids with a protein, each combination having a different response intensity and response range to the aldehyde levels. If desired, the composition can be adjusted to detect and measure a specific concentration of aldehyde. The color differentiations between different concentrations of aldehyde are excellent, therefore, the composition can be used in a quantitative test, rather than qualitative, test.

[0116] In accordance with an important feature of the present invention, the continuing and substantial problems in dry phase test strips for quantitatively assaying a sample for high concentrations of aldehydes are essentially eliminated. An indicator reagent composition of the present invention provides a differentiable response to the aldehyde concentration over a range of 0% to greater than about 4%, and particularly about 0.5% to greater than about 4%, by weight of the sample. Therefore, accurate and reliable assays for aldehyde content in undiluted samples can be performed by utilizing an indicator reagent composition and device of the present invention.

### EXAMPLE III

[0117] A 10% solution of DL-lysine free base was prepared with water. A water-soluble polymer, hydroxyethylcellulose, was prepared as a premixed 2.5% solution. The hydroxyethylcellulose solution was added to the reagent solution to obtain a final concentration of 0.25%, by weight, by replacing the equivalent volume of water. The final mixture of reagent solution was applied to filter paper, such as Schleicher & Schull #903 absorption paper, and immersed in a solution to impregnate solution components onto the paper. The impregnated filter paper was dried in a forced-air oven at 65°C for 15 min. until the paper was dry. The dried reagent paper was assembled into a reagent strip by cutting the reagent paper into a 0.2 inch ribbon and adhering the paper to the long edge of a 2.5 inch wide polystyrene plastic sheet with a double sided adhesive. The reagent paper attached plastic sheet then was cut into 0.2 inch wide strips. The final strips had a 0.2 x 0.2 square inch reagent paper attached to a 0.2 x 2.5 plastic handle.

[0118] To test the color response of the reagent strip to various glutaraldehyde solutions, a stock solution of 25% glutaraldehyde, by weight, was diluted to 1, 2, 3, and 4%, by weight, respectively, with deionized water. The strips were dipped into the glutaraldehyde solution for one second, the excess solution was removed by touching the edge of the strip with a clean tissue paper. The strongest strip color response was obtained between 60 and 120 seconds. The color response of each impregnated strip is shown below in Table 9.



Table 9

Color response of reagent strips containing lysine-based indicator reagent composition for increasing glutaraldehyde concentration	
Glutaraldehyde Concentration	Color Response of Dry Reagent Strip
1%	Yellow
2%	Orange
3%	Pumpkin
4%	Reddish Brown

**EXAMPLE IV**

[0119] Dry reagent test strips were prepared with arginine and tested for color response to glutaraldehyde concentrations from 1 to 10%, by weight. The arginine-based reagent strips were prepared using similar procedures for preparing the above lysine-based reagent strips, but substituting arginine for lysine. A stock solution of 25% glutaraldehyde, by weight, was diluted with deionized water to concentrations of 1%, 3%, 5%, and 10%, by weight, to give a series of test solutions. The test solutions were tested with the prepared strips and the results are reported below in Table 10.

Table 10

Color response of reagent strips containing arginine-based indicator reagent composition for increasing glutaraldehyde concentration	
Glutaraldehyde Concentration	Color Response of Dry Reagent Strip
1%	Yellow
3%	Orange
5%	Pumpkin
10%	Reddish Brown

[0120] The data in Tables 9 and 10 demonstrate an indicator reagent composition containing a diamino carboxylic acid provides a distinct color response for each different concentration of dialdehyde. More particularly, the data shows that an indicator reagent composition can be formulated containing one or more mixtures of different diamino carboxylic acids to provide a desired color response in the range of from about 0.5% to about 15%, by weight. In particular, the color transition was different for each concentration of glutaraldehyde.

[0121] The indicator reagent composition containing the diamino carboxylic acid can be used to generate a color response in the strip that correlates to the amount of glutaraldehyde present in the sample, and thereby quantitatively determine the glutaraldehyde concentration in a sample. The improved ability to differentiate a particular concentration of glutaraldehyde is an important advantage for identifying and quantifying the dialdehyde content in a sample, and is quite unexpected in light of the present state of the art.

[0122] In accordance with an important feature of the present invention, the continuing and substantial problems in dry phase test strips for quantitatively assaying a sample for high concentrations of aldehydes, including monoaldehydes and dialdehydes, are essentially eliminated. An indicator reagent composition of the present invention provides a differentiable response to the dialdehyde concentration over a range of 0% to about 20%, and particularly about 0.5% to about 6%, by weight of the sample. Therefore, accurate and reliable assays for dialdehyde content in undiluted samples can be performed by utilizing an indicator reagent composition and device of the present invention.

[0123] Modifications and variations of the invention as hereinbefore set forth can be made without departing from the spirit and scope thereof, and, therefore, only such limitations should be imposed as are indicated by the appended claims.

[0124] The features disclosed in the foregoing description and in the claims may, both separately and in any combination thereof, be material for realising the invention in diverse forms thereof.

## Claims

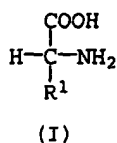
1. A composition capable of exhibiting a detectable and measurable color transition in response to a concentration of 0% to greater than 4%, by weight, of an aldehyde, said composition comprising:

(a) a protein;  
 (b) an amine;  
 (c) a color indicator;  
 (d) an optional polymer; and  
 (e) a carrier comprising water.

2. The composition of claim 1 wherein the protein comprises bovine serum albumin, human serum albumin, ovalbumin, gamma globulin, or a mixture thereof.

3. The composition of claim 1 wherein the protein is present in an amount of about 1% to about 25%, by weight of the composition.

4. The composition of claim 1 wherein the amine is an amino acid or a peptide comprising at least two amino acids of the formula:



wherein R<sup>1</sup> is hydrogen or alkyl, optionally substituted with amino, guanidino, carboxy, hydroxy, ureido, or sulfhydryl.

5. The composition of claim 4 wherein the amino acid comprises alanine, asparagine, glycine, lysine, arginine, aspartic acid, glutamic acid, cysteine, serine, ornithine, citrulline, threonine, or a mixture thereof.

6. The composition of claim 4 wherein the peptide comprises two to about five amino acids.

7. The composition of claim 4 wherein the peptide comprises glycylglycine.

8. The composition of claim 1 wherein the amine is present in an amount of about 5% to about 25%, by weight of the composition.

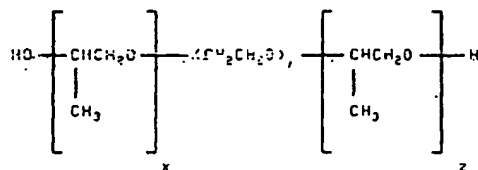
9. The composition of claim 1 wherein the optional polymer is a nonionic polymer.

10. The composition of claim 9 wherein the polymer comprises a water-soluble, cellulose-based polymer.

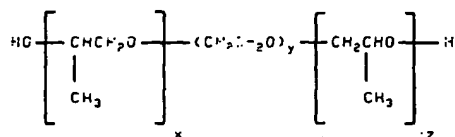
11. The composition of claim 9 wherein the cellulose-based polymer is selected from the group consisting of methylcellulose, hydroxymethylcellulose, hydroxyethylcellulose, hydroxyethylmethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose, carboxymethylcellulose and salts thereof, hydroxybutylcellulose, cellulose acetate, carboxymethylhydroxyethylcellulose, hydroxybutylmethylcellulose, and mixtures thereof.

12. The composition of claim 9 wherein the polymer comprises hydroxyethylcellulose.

13. The composition of claim 9 wherein the polymer comprises a water-soluble polymer selected from the group consisting of polyvinylpyrrolidone, hydrolyzed polyvinylpyrrolidone, poly(vinyl alcohol), poly(vinyl acetate), vinyl acetatevinyl alcohol copolymer, poly(methacrylamide), a polyoxypropylenepolyoxyethylene block polymer having a structure:



or

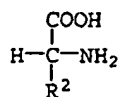


wherein x and z, independently, are an integer from about 4 to about 30, and y is an integer from about 4 to about 100, polyacrylamide, a vinyl alcohol copolymer, and mixtures thereof.

14. The composition of claim 1 wherein the polymer comprises an amount of 0.1% to about 5%, by weight of the composition.
15. The composition of claim 1 further comprising a nonionic or anionic surfactant.
16. The composition of claim 15 wherein the surfactant is selected from the group consisting of an ethoxylated polysorbate, an ethoxylated alcohol, an ethoxylated phenol, a polyethylene glycol, a polypropylene glycol, an ethylene glycolpropylene glycol copolymer, an alkyl sulfate, an alkyl ether sulfate, an alkyl ether sulfonate, a sulfate ester of an alkylphenoxy polyoxyethylene ethanol, an alphaolefin sulfonate, a beta-alkyloxy alkane sulfonate, an alkyl arylsulfonate, an alkyl carbonate, an alkyl ether carboxylate, a fatty acid, a sulfosuccinate, an alkyl ether sulfosuccinate, a sarcosinate, an octoxynol phosphate, a nonoxynol phosphate, a taurate, a fatty tauride, a sulfated monoglyceride, a fatty acid amido polyoxyethylene sulfate, and mixtures thereof.
17. The composition of claim 1 comprising:
  - (a) about 1% to about 25% by weight protein;
  - (b) about 5% to about 25% by weight amino acid or peptide;
  - (c) about 0.005% to about 0.05% by weight color indicator; and
  - (d) about 0.1% to about 5% by weight of a polymer selected from the group consisting of hydroxypropylcellulose, hydroxyethylcellulose, methylcellulose, hydroxymethylcellulose, carboxymethylcellulose, polyvinylpyrrolidone, and mixtures thereof.
18. The composition of claim 1 wherein the carrier further comprises an organic solvent.
19. The composition of claim 1 wherein the composition has a pH of from about 5 to about 11.
20. The composition of claim 1 wherein the color indicator is selected from the group consisting of bromphenol blue, tetrabromophenol blue, Congo red, methyl orange, bromchlorophenol blue, p-ethoxychrysoidine, alpha-naphthyl red, sodium alizarinsulfonate, bromcresol green, 2,5-dinitrophenol, methyl red, lacmoid, litmus, chlorophenol red, benzoyl auramine G, azolitmin, bromcresol purple, bromphenol red, dibromophenol-tetrabromophenol-sulfonphthalein, p-nitrophenol, bromothymol blue, phenol red, neutral red, rosolic acid aurin, quinoline blue, cresol red, alphanaphtholphthalein, metacresol purple, ethyl bis[2,4-dinitrophenyl]acetate, tropaeolin, thymol blue, o-cresolphthalein, phenolphthalein, thymolphthalein, Nile blue A, alpha-naphtholbenzein, alizarin yellow GG, alizarin yellow R, and mixtures thereof.

21. A method of determining aldehyde content of a sample containing 0% to greater than 4% by weight aldehyde, said method comprising:
- 5 (a) contacting the sample with an indicator reagent composition comprising:
- (i) a protein,  
(ii) an amine,  
(iii) a color indicator, and  
10 (iv) an optional polymer; and
- (b) determining the aldehyde content of the sample from the intensity and degree of a color transition of the indicator reagent composition.
22. The method of claim 21 wherein the sample has an aldehyde content of 0.5% to greater than 4% by weight aldehyde.
23. The method of claim 21 wherein the aldehyde is glutaraldehyde or formaldehyde.
24. The method of claim 21 wherein the intensity and degree of the color transition are determined visually or instrumentally.
- 20 25. The method of claim 21 wherein the amine is an amino acid or a peptide.
26. The method of claim 21 wherein the sample is an aqueous sample or a gaseous sample.
27. A method of quantitatively determining the aldehyde content of a sample containing 0% to greater than 4% by weight aldehyde, said method comprising:
- 30 (a) contacting the sample with an analyte detection device comprising a test pad, said test pad having incorporated therein an indicator reagent composition comprising a carrier matrix impregnated with a solution comprising:
- (i) a protein,  
(ii) an amine,  
35 (iii) a color indicator, and  
(iv) an optional polymer; and
- (b) examining the analyte detection device for a color transition; and  
(c) correlating the color transition to the aldehyde content of the aqueous sample.
- 40 28. An analyte-detection device to determine the aldehyde content of an aqueous sample comprising:
- a support strip;  
a test pad; and  
45 an indicator reagent composition incorporated into the test pad, said reagent composition comprising:
- (a) a protein,  
(b) an amine,  
(c) a color indicator, and  
50 (d) an optional polymer.
29. A composition capable of exhibiting a detectable and measurable color transition in response to a concentration of 0% to about 20%, by weight, of a dialdehyde, said composition comprising:
- 55 (a) a diamino carboxylic acid;  
(b) a water-soluble polymer; and  
(c) a carrier comprising water.

30. The composition of claim 29 wherein the diamino carboxylic acid has a formula:



(II)

wherein  $\text{R}^2$  is alkyl substituted with amino, amido, guanidino, or ureido, and further optionally substituted with hydroxy.

31. The composition of claim 29 wherein the diamino carboxylic acid is selected from the group consisting of lysine, ornithine, L-2,3-diaminopropionic acid, L-2,3-diaminobutyric acid, arginine, canavanine, hydroxylysine, asparagine, glutamine, and mixtures thereof.

32. The composition of claim 29 wherein the diamino carboxylic acid is lysine, ornithine, arginine, or a mixture thereof.

33. The composition of claim 29 wherein the diamino carboxylic acid is present in an amount of about 1% to about 25%, by weight of the composition.

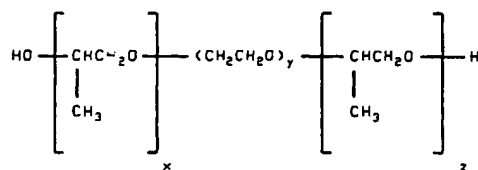
34. The composition of claim 29 wherein the water-soluble polymer comprises a nonionic polymer.

35. The composition of claim 34 wherein the polymer comprises a cellulose-based polymer.

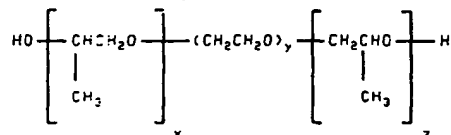
36. The composition of claim 34 wherein the cellulose-based polymer is selected from the group consisting of methylcellulose, hydroxymethylcellulose, hydroxyethylmethylcellulose, hydroxypropylmethylcellulose, carboxymethylcellulose and salts thereof, hydroxybutylcellulose, cellulose acetate, carboxymethylhydroxyethylcellulose, hydroxybutylmethylcellulose, and mixtures thereof.

37. The composition of claim 34 wherein the polymer comprises hydroxyethylcellulose.

38. The composition of claim 34 wherein the polymer is selected from the group consisting of polyvinylpyrrolidone, hydrolyzed polyvinylpyrrolidone, poly(vinyl alcohol), poly(vinyl acetate), vinyl acetate-vinyl alcohol copolymer, poly(methacrylamide), a polyoxypropylene-polyoxyethylene block polymer having a structure:



or



wherein x and z, independently, are an integer from about 4 to about 30, and y is an integer from about 4 to about 100, polyacrylamide, a vinyl alcohol copolymer, and mixtures thereof.

39. The composition of claim 34 wherein the polymer is present in an amount of 0.1% to about 5%, by weight of the composition.

40. The composition of claim 29 further comprising a nonionic or anionic surfactant.

41. The composition of claim 40 wherein the anionic surfactant is selected from the group consisting of an ethoxylated polysorbate, an ethoxylated alcohol, an ethoxylated phenol, a polyethylene glycol, a polypropylene glycol, an ethylene glycol-propylene glycol copolymer, an alkyl sulfate, an alkyl ether sulfate, an alkyl ether sulfonate, a sulfate ester of an alkylphenoxy polyoxyethylene ethanol, an alpha-olefin sulfonate, a beta-alkyloxy alkane sulfonate, an alkyl arylsulfonate, an alkyl carbonate, an alkyl ether carboxylate, a fatty acid, a sulfosuccinate, an alkyl ether sulfosuccinate, a sarcosinate, an octoxynol phosphate, a nonoxynol phosphate, a taurate, a fatty tauride, a sulfated monoglyceride, a fatty acid amido polyoxyethylene sulfate, and mixtures thereof.

42. The composition of claim 29 comprising:

- (a) about 1% to about 25% by weight diamino carboxylic acid; and
- (b) about 0.1% to about 5% by weight of a polymer selected from the group consisting of hydroxypropylcellulose, hydroxyethylcellulose, methylcellulose, hydroxymethylcellulose, carboxymethylcellulose, polyvinylpyrrolidone, and mixtures thereof.

43. The composition of claim 29 wherein the carrier further comprises an organic solvent.

44. A method of determining a dialdehyde content of a sample containing 0% to about 20% by weight of the dialdehyde, said method comprising:

- (a) contacting the sample with an indicator reagent composition comprising:
  - (i) a diamino carboxylic acid, and
  - (ii) an optional polymer; and
- (b) determining the dialdehyde content of the sample from the intensity and degree of a color transition of the indicator reagent composition.

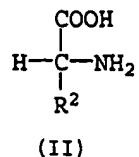
45. The method of claim 44 wherein the sample has a dialdehyde content of about 0.5% to about 6% by weight dialdehyde.

46. The method of claim 44 wherein the dialdehyde is selected from the group consisting of oxalaldehyde, malonaldehyde, succinaldehyde, glutaraldehyde, and adipaldehyde.

47. The method of claim 44 wherein the dialdehyde is glutaraldehyde.

48. The method of claim 44 wherein the intensity and degree of the color transition are determined visually or instrumentally.

49. The method of claim 44 wherein the diamino carboxylic acid has a formula:



wherein R<sup>2</sup> is alkyl substituted with amino, amido guanidino, or ureido, and further optionally substituted with hydroxy.

50. The method of claim 44 wherein the sample is an aqueous sample or a gaseous sample.

51. A method of quantitatively determining the dialdehyde content of a sample containing 0% to about 20% by weight of the dialdehyde, said method comprising:

(a) contacting the sample with an analyte detection device comprising a test pad, said test pad having incorporated therein an indicator reagent composition comprising a carrier matrix impregnated with a solution comprising:

- (i) a diamino carboxylic acid, and
- (ii) an optional polymer; and

(b) examining the analyte detection device for a color transition; and  
 (c) correlating the color transition to the dialdehyde content of the aqueous sample.

52. An analyte-detection device to determine a dialdehyde content of an aqueous sample comprising:

a support strip;  
 a test pad adhering to the support strip; and  
 an indicator reagent composition incorporated into the test pad, said reagent composition comprising:

- (a) a diamino carboxylic acid, and
- (d) an optional polymer.